



NIMH Study to Examine Effects of Depression Treatment on Microbiome-Gut-Brain Axis Among People Living With HIV

The National Institute of Mental Health has awarded a five-year, \$5.4 million grant to investigators at the University of Miami and University of Missouri – St. Louis to conduct research on the microbiome-gut-brain (MGB) axis in people with co-occurring HIV and depression.



Adam Carrico, Ph.D.

The study, Treatment Research Investigating Depression Effects on Neuroimmune Targets (TRIDENT), will examine the effect of treating depression on MGB axis pathways in people living with HIV (PLWH). To lower depression among PLWH, an evidence-based treatment for depression and poor adherence to HIV/AIDS antiretroviral therapy known as CBT-AD (cognitive-behavioral therapy for adherence and depression treatment) will be administered.



“We have assembled a strong team with expertise in the microbiome, gene expression, and neuroHIV to understand how CBT-AD-related reductions in depression could influence different aspects of the MGB axis in PLWH,” said Adam Carrico, Ph.D., professor of public health sciences and psychology, who will serve as principal investigator. Dr. Carrico also directs the Prevention Science and Community Health Division in the Miller School’s Department of Public Health Sciences.

People living with HIV experience damage to the gastrointestinal tract during acute HIV infection. These pathologies result in immune dysregulation through dysbiosis – an imbalance of the microflora within the gut – and translocation of inflammatory microbial products into the periphery. This syndrome, in turn, is known to heighten the risk for depression and other neuropsychiatric disorders in PLWH.

To improve depression treatment for PLWH, clinical research is needed to advance scientific understanding of MGB axis interactions. TRIDENT will utilize fMRI to examine the underlying mechanisms taking place during HIV infection among the microbiome, gastrointestinal tract, immune system, and brain function.

Approximately 150 participants will be enrolled in the randomized controlled trial. Some participants will receive the CBT-AD treatment; the study population will also include a wait-list control (WLC) group. CBT-AD participants will receive up to 12 individual sessions of treatment over four months. WLC participants will provide important comparative results and will have the opportunity to receive CBT-AD after six months.



Periodic assessments will evaluate treatment effects such as changes in the microbiome, soluble immune markers relevant to HIV immunology, and leukocyte signaling to measure the conserved transcriptional response to adversity (CTRA). All participants will complete a final follow-up assessment 10 months after implementation of the trial.



Steven Safren,
Ph.D.

In addition to Dr. Carrico, principal investigators include Steven Safren, Ph.D., professor at the University of Miami Department of Psychology and director of the UM Center for HIV and Research in Mental Health; and Robert Paul, Ph.D., professor of behavioral medicine at the University of Missouri – St. Louis and director of the Missouri Institute of Mental Health.

“I am excited to have been invited to join this stellar team and be able to use our evidence-based depression treatment [CBT-AD] to learn how improved depression will affect the MGB axis,” Dr. Safren said.

“This study will break new ground by leveraging a unique clinical trial design and novel analytic strategies to



delineate the complex interplay between peripheral and central mechanisms that underlie mood disorders among PLWH,” Dr. Paul said. “Our findings will have direct clinical relevance and high potential to improve life quality and overall health among PLWH.”



Roger McIntosh,
Ph.D

The primary outcomes of task-based activation and resting state connectivity of the negative valence system will be derived from fMRI scans to be conducted on the Coral Gables campus by co-investigator Roger McIntosh, Ph.D., associate professor at the University of Miami Department of Psychology.

“Understanding temporal dynamics of the mind-body connection and the extent to which CBT-AD contributes to functional brain changes under different conditions – e.g., resting, interoception, and emotional regulation – may be important for the overall disease management in PLWH,” Dr. McIntosh said.

TRIDENT will generate multi-level, high-dimensional data on the MGB axis among people with co-occurring HIV and depression. Study results will guide the development of new pharmacologic and behavioral treatments for depression and its



neurobehavioral substrates in PLWH.

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